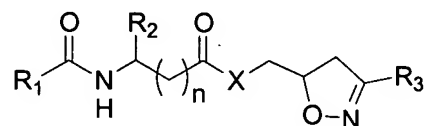


WHAT IS CLAIMED IS:

1. A method of treating Celiac Sprue and/or dermatitis herpetiformis, the method comprising:  
administering to a patient an effective dose of a tTGase inhibitor;  
wherein said tTGase inhibitor attenuates gluten toxicity in said patient.
2. The method of Claim 1, wherein said tTGase inhibitor is or comprises a dihydroisoxazole moiety or is an analog of isatin.
3. The method of Claim 1, wherein said tTGase inhibitor is administered with a glutenase.
4. The method according to Claim 1, wherein said tTGase inhibitor is administered orally.
5. The method according to Claim 1, wherein said tTGase inhibitor is contained in a formulation that comprises an enteric coating.
6. A formulation for use in treatment of Celiac Sprue and/or dermatitis herpetiformis, comprising:  
an effective dose of a tTGase inhibitor and a pharmaceutically acceptable excipient.
7. The formulation of Claim 6, wherein said tTGase inhibitory moiety is:



wherein R<sub>1</sub> and R<sub>2</sub> are independently selected from H, alkyl, alkenyl, cycloalkyl, aryl, heteroalkyl, heteroaryl, alkoxy, alkylthio, arakyl, aralkenyl, halo, haloalkyl, haloalkoxy, heterocyclyl, and heterocyclylalkyl groups, an amino acid, a peptide, a peptidomimetic, or a peptidic protecting group; wherein R<sub>2</sub> can additionally be selected from the group consisting of LPYPQPQLPY, LPFPQPQLPF-NH<sub>2</sub>, LPYPQPQLP, LPYPQPQLPYQPQPFP, LP-X<sub>2-15</sub>, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a C-terminal proline;

R<sub>3</sub> is selected from F, I, Cl, and Br; n is from 0 to 10; and X is selected from the group consisting of O and NH.

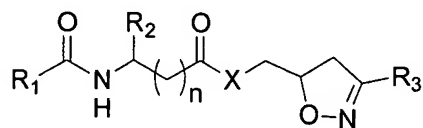
8. The formulation of Claim 7, wherein R<sub>1</sub> is selected from the group consisting of BnO, Me, Cbz, Fmoc, Boc, PQP, Ac-PQP, PQPQLPYPQP, Ac-PQPQLPFPQP, QLQPFPQP, LQLQPFPQPLPYPQP, X<sub>2-15</sub>-P, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a N-terminal proline.

9. The formulation of Claim 7, wherein R<sub>2</sub> is selected from the group consisting of (S)-Bn, (S)-CO<sub>2</sub>Me, (S)-Me, (R)-Bn, (S)-CH<sub>2</sub>CONHBn, (S)-(1*H*-indol-yl)-methyl, (S)-(4-hydroxyphenyl)-methyl, OMe, OtBu, Gly, Gly-NH<sub>2</sub>, LPY, LPF-NH<sub>2</sub>.

10. The formulation inhibitor of Claim 7, wherein said tTGase inhibitor is selected from the group consisting of:

{(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; (S)-2-Benzyloxycarbonylamino-4-[(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-butyric acid methyl ester; (S)-2-Benzyloxycarbonylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-succinamic acid methyl ester; (S)-2-Benzyloxycarbonylamino-3-phenyl-propionic acid 3-bromo-4,5-dihydro-isoxazol-5-ylmethyl ester; {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; (S)-2-Acetylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-3-phenyl-propionamide; {(R)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; {(S)-2-Benzylcarbamoyl-1-[(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid benzyl ester; {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; and [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid benzyl ester.

11. The method according to Claim 1, wherein said tTGase inhibitor has the formula:



wherein  $R_1$  and  $R_2$  are independently selected from H, alkyl, alkenyl, cycloalkyl, aryl, heteroalkyl, heteroaryl, alkoxy, alkylthio, arakyl, aralkenyl, halo, haloalkyl, haloalkoxy, heterocyclyl, and heterocyclylalkyl groups, an amino acid, a peptide, a peptidomimetic, or a peptidic protecting group; wherein  $R_2$  can additionally be selected from the group consisting of LPYPQPQLPY, LPFPQPQLPF-NH<sub>2</sub>, LPYPQPQLP, LPYPQPQLPYQPQPF, LP-X<sub>2-15</sub>, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a C-terminal proline;  $R_3$  is selected from F, I, Cl, and Br; n is from 0 to 10; and X is selected from the group consisting of O and NH.

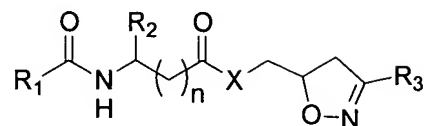
12. The method of Claim 11, wherein  $R_1$  is selected from the group consisting of BnO, Me, Cbz, Fmoc, Boc, PQP, Ac-PQP, PQPQLPYPQP, Ac-PQPQLPFPQP, QLQPFQP, LQLQPFQPPLPYPQP, X<sub>2-15</sub>-P, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a N-terminal proline.

13. The method of Claim 11, wherein  $R_2$  is selected from the group consisting of (S)-Bn, (S)-CO<sub>2</sub>Me, (S)-Me, (R)-Bn, (S)-CH<sub>2</sub>CONHBn, (S)-(1*H*-indol-yl)-methyl, (S)-(4-hydroxyphenyl)-methyl, OMe, OtBu, Gly, Gly-NH<sub>2</sub>, LPY, LPF-NH<sub>2</sub>.

14. The method according to Claim 11, wherein said TGase inhibitor is selected from the group consisting of:

{{(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; (S)-2-Benzyloxycarbonylamino-4-[(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-butyric acid methyl ester; (S)-2-Benzyloxycarbonylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-succinamic acid methyl ester; (S)-2-Benzyloxycarbonylamino-3-phenyl-propionic acid 3-bromo-4,5-dihydro-isoxazol-5-ylmethyl ester; {{(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; (S)-2-Acetylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-3-phenyl-propionamide; {{(R)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; {{(S)-2-Benzylcarbamoyl-1-[(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-(1*H*-indol-3-yl)-ethyl}-carbamic acid benzyl ester; {{(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; and [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-(4-hydroxy-phenyl)-ethyl}-carbamic acid benzyl ester.

15. A tTGase inhibitor of the formula:



wherein  $R_1$  and  $R_2$  are independently selected from H, alkyl, alkenyl, cycloalkyl, aryl, heteroalkyl, heteroaryl, alkoxy, alkylthio, arakyl, aralkenyl, halo, haloalkyl, haloalkoxy, heterocyclyl, and heterocyclalkyl groups, an amino acid, a peptide, a peptidomimetic, or a peptidic protecting group; wherein  $R_2$  can additionally be selected from the group consisting of LPYPQPQLPY, LPFPQPQLPF-NH<sub>2</sub>, LPYPQPQLP, LPYPQPQLPYPQPQPF, LP-X<sub>2-15</sub>, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a C-terminal proline;  $R_3$  is selected from F, I, Cl, and Br;  $n$  is from 0 to 10; and  $X$  is selected from the group consisting of O and NH,

other than {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester.

16. The tTGase inhibitor of Claim 15, wherein  $R_1$  is selected from the group consisting of BnO, Me, Cbz, Fmoc, Boc, PQP, Ac-PQP, PQPQLPYPQP, Ac-PQPQLPFPQP, QLQFPQP, LQLQFPQPPLPYPQP, X<sub>2-15</sub>-P, where X<sub>2-15</sub> is a peptide consisting of any 2-15 amino acid residues followed by a N-terminal proline.

17. The tTGase inhibitor of Claim 15, wherein  $R_2$  is selected from the group consisting of (S)-Bn, (S)-CO<sub>2</sub>Me, (S)-Me, (R)-Bn, (S)-CH<sub>2</sub>CONHBn, (S)-(1*H*-inol-yl)-methyl, (S)-(4-hydroxy-phenyl)-methyl, OMe, OtBu, Gly, Gly-NH<sub>2</sub>, LPY, LPF-NH<sub>2</sub>.

18. The tTGase inhibitor of Claim 15, wherein said tTGase inhibitor is selected from the group consisting of:

(S)-2-Benzoyloxycarbonylamino-4-[(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-butyric acid methyl ester; (S)-2-Benzoyloxycarbonylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-succinamic acid methyl ester; (S)-2-Benzoyloxycarbonylamino-3-phenyl-propionic acid 3-bromo-4,5-dihydro-isoxazol-5-ylmethyl ester; {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; (S)-2-Acetylamino-*N*-(3-bromo-4,5-dihydro-isoxazol-5-ylmethyl)-3-phenyl-propionamide; {(R)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester; {(S)-2-Benzylcarbamoyl-1-[(3-bromo-

4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-ethyl}-carbamic acid benzyl ester; [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid benzyl ester; {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-phenylethyl}-carbamic acid benzyl ester; and [(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-methyl-carbamoyl]-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid benzyl ester.